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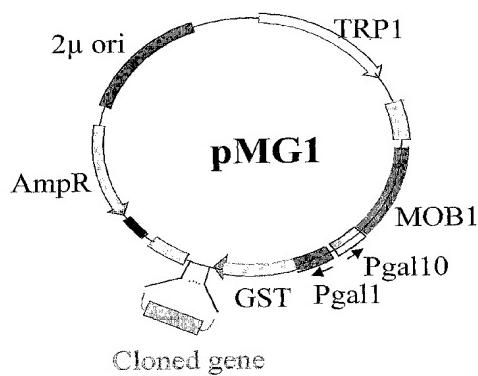
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(54) Title: SELECTION MARKERS USEFUL FOR HETEROLOGOUS PROTEIN EXPRESSION



(57) Abstract: Selection markers in prior art systems are based on resistance genes or on complementation of auxotrophic mutations. The requirement for expression of these markers is conditional e.g. on the presence of an antibiotic, or on the absence of a nutrient. In contrast, the selection markers used in this invention are non-conditional, and selection pressure is absolute. The markers involved are genes which encode essential survival factors, such that loss of the marker gene is lethal. Thus the invention provides a cell which expresses chromosomal genes and extra-chromosomal genes, wherein (a) the expressed extra-chromosomal genes include an essential gene whose expression is unconditionally required for survival of the cell, (b) the expressed chromosomal genes do not include said essential gene, and (c) the extra-chromosomal genes include a heterologous gene. The cells can conveniently be obtained by a plasmid shuffling procedure.

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SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
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